

controls. Thus, using the 954 patients, all of the differences in risk factors that exist between cases and controls are due to age, not disease status. All of these patients are high risk and the younger patients have not yet shown clinical manifestation of cardiovascular disease.

Using a subset of age matched cases (N=173, means 60 yr.) and controls (N=173, means 59 yr.) between 54 and 66 years of age, the cases had significantly:

Higher homocysteine (9.7 vs. 8.7,  $P<0.01$ ), and Lower TC (179 vs. 201,  $p<0.0001$ ), LDLC (107 vs. 121,  $p<0.001$ ), triglyceride (140 vs. 163,  $p<0.05$ ), apoA1 (112 vs. 123,  $p<0.01$ ) apoB (85 vs. 96,  $p<0.001$ ), and TC/HDL2b (14.8 vs. 20.2,  $p<0.05$ ). These data indicate that the cases are more aggressively treated with medications than the controls.

Using a subset of age-matched cases (N=146, mean 55 yr.) and controls (N=93, mean 55 yr.) between 44 and 66 years of age without hyperlipidemia, the cases had:

Higher HDL3b (19.9 vs. 17.9,  $p<0.05$ ), HDL3 (58.8 vs. 55.7,  $p=0.08$ ) and LDLII+IV/HDL2+3 (0.40 vs. 0.38,  $p=0.11$ ), and

Lower TC (182 vs. 205,  $p<0.001$ ), LDLC (109 vs. 124,  $p<0.01$ ), HDLC (44 vs. LDL11A (16.8 vs. 18.2,  $p=0.09$ ), HDL2b (15.5 vs. 18.6,  $p<0.05$ ), and HDL2 (41.3 vs. 44.5,  $p=0.06$ ). These data again indicate that cases may be more aggressively treated with medications than the controls, even though they do not have hyperlipidemia. These data also indicate some important risk factors in the cases: a higher ratio of small LDL to HDL, small LDL size and lower HDL2b.

These data illustrate the value of the cardiovascular informatic knowledge base in deriving heretofore unrecognized relationships between data, especially highly discriminating lipoprotein subfractions, in diagnosing risk factors which may govern the treatment of patients.

We note that this data is based on 948 patients. Because the percentage distribution of LDL and HDL subclass data can be stored, the LDL and HDL subclass database is now based on over 100,000 patients and provides for insight on the relationship of LDL and HDL subclass particle

percentage distribution not previously known to the art, as well as, accuracy in risk assessment, diagnosis and treatment unavailable in the art.

Also see particle size and percent distribution of HDL subparticles in figures 5 and 15 provides a patient cardiovascular profile. Figure 23 shows LDL and HDL subparticle data in relationship to coronary risk and disease factors and cardiovascular therapy.

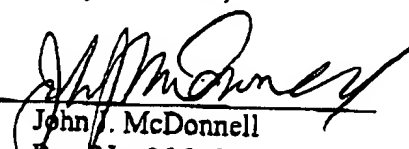
The use of percentage distribution LDL and HDL subclass particle data in the cardiovascular healthcare management system of the present invention provides cardiovascular risk factor assessment, diagnosis and management which is not obtainable in any prior art system. The comparison of patients LDL and HDL subclass particle distribution results to stored LDL and HDL subclass data provides truly unobvious risk assessment, diagnosis and treatment of patients that is not contemplated or achievable by the prior art.

The cardiovascular management system is configured to present the data to remote physicians and provides for the physician interacting with the patient.

Allowance of claims 21-34 are earnestly solicited.

Respectfully submitted,

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